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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,458	10/20/2003	Alfred M. Ajami	3287,1000-003	4844

21005 7590 11/16/2004

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EXAMINER

HUANG, EVELYN MEI

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/690,458	<b>Applicant(s)</b> AJAMI ET AL.	
	<b>Examiner</b> Evelyn Huang	<b>Art Unit</b> 1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 August 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-27 and 30-39 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-27,30-32,34,35 and 37-39 is/are rejected.
- 7) ☒ Claim(s) 33, 36 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

1. Claims 1-27, 30-39 are pending. Claims 28, 29 have been canceled according to the amendment filed on 8-16-2004.

#### *Claim Rejections - 35 USC § 112*

2. The rejection for Claims 1-29 under 35 U.S.C. 112 second paragraph is withdrawn because the amendment has obviated the rejection.

#### *Claim Rejections - 35 USC § 103*

3. The rejection for Claims 1-29 under 35 U.S.C. 103(a) as being unpatentable over Brana I (4204063, PTO-1449) in view of Brana II (5420137, PTO-1449), Berge (Journal of Pharmaceutical Sciences, 1977, 66(1); 1-19) and Zee-Cheng (4614820) is maintained for reasons of record. The rejection is applicable to new claims 30-32, 34-35, 37-39.

Applicant argues that the ease of purification of the salts of the present invention as shown in Table 3 is unexpected and thereby rendering the instant non-obvious over the prior art of record.

However, ease of purification is not an innate property of the compound. It is dependent on a combination of factors, such as the solvents, the operating conditions etc. The results under different conditions as shown in Table 3 therefore fail to render the inventive compound unobvious over the prior art compound, since unexpected properties must be compared on a vis-à-vis basis, and no generalization can be concluded.

Furthermore, Table 3 shows that the purity of the instant carboxylic acid salts after 1x crystallization ranges from 97 to 99.6%, whereas the purity of the non-carboxylic acid salts ranges from 92-99.2%. Thus there is an overlap in range. In the absence of statistical analysis in a side-by-side comparison, distinction between these two ranges cannot be concluded. Unexpected results therefore has not been established, the instant remains obvious over the prior art of record.

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The comparative data presented in Table 4 (pages 31-32 of the specification) fails to render the instant over the prior art of record for the following reasons. While some of the amonafide organic acid salt of the instant are more soluble in distilled water and in saline at high concentration than the corresponding HCl salt, such a result is not unexpected as it is well recognized in the art that organic acid salts of basic drugs, such as amines, were more soluble in water than the corresponding inorganic (halide) salts (Berge et al. 1977, Journal of Pharmaceutical Sciences, 66(1); 1-19). Indeed, Brana's methansulfonic salt at high concentration is soluble both in saline and distilled water (as shown on page 29 of the specification) and is more soluble than some of the instant carboxylic acid salts. The various carboxylic acid salts of amonafide (tartrate, malonate, citrate, succinate, fumarate or maleate etc) in the Table have similar solubility among themselves, and are similar to the amonafide methansulfonic acid salt of Brana. The instant claims directed to the amonafide carboxylic acid salts or the malic or glycolic acid salts of the non-amonafide compound embraced in the generic claims therefore remain obvious over the prior art of record since unexpected results have not been established for these claims.

#### ***Claim Rejections - 35 USC § 112***

4. The enablement rejection for Claims 20-29 under 35 U.S.C. 112, first paragraph, is withdrawn the claims have been amended to the method of treating leukemia, breast, colon, lung or prostate cancer, which find support on pages 33-38 of the specification and in Figures 2-10.

#### ***Double Patenting***

5. The timely filed terminal disclaimer has obviated the rejection for Claims 11-29 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 27 of U.S. Patent No. 6693198 in view of Brana I (4204063, PTO-1449).

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*Allowable Subject Matter*

6. Claims 33, 36, directed to the composition and method of use of amonafide malate, (amonafide malate has been allowed in the parent application) are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

*Conclusion*

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

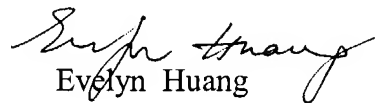
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Evelyn Huang

Primary Examiner

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